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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,181	11/10/1999	Snezna Rogelj	UNME-0054-1	7645

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EXAMINER	
LUKTON, DAVID	
ART UNIT	PAPER NUMBER
1653	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/424,181	Applicant(s) ROGELJ ET AL.	
	Examiner David Lukton	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-35* is/are pending in the application.

4a) Of the above claim(s) *9,10,12-20,27,34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8,11,21-26 and 28-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Pursuant paper No. 19 (filed 6/24/02), claim 1 has been cancelled, and claims 2-8 and 11 amended. Claims 2-35 remain pending. Claims 21-26, 28-33 are now rejoined with the elected group. Claims 2-8, 11, 21-26, 28-33 are examined in this Office action; claims 9, 10, 12-20, 27, 34-35 remain withdrawn from consideration.

Applicants' arguments filed 3/13/02 have been considered and found persuasive in part. The rejections of claim 1 are rendered moot by cancellation of this claim.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-8, 11, 21-26, 28-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejected claims are drawn to a method of inhibiting PDI or to a method of treating a viral infection. It appears from figure 3 that PAO* [*para*-N-(ethane-2-sulfonic acid)amino phenylarsenoxide] exhibited inhibition of L-selectin shedding. In addition, on page 21, line 19, it is asserted that PAO* exhibited anti-HIV activity in an assay which might have

been the same as that described in Weislow (*J Natl Cancer Inst* **81**, 577, 1989), or it may have been different therefrom. However, no results were presented, and so it is not possible to determine what activity this compound might have exhibited, or even what the assay was. It is also not possible to determine what control experiments might have been carried out. If ostensibly inactive compounds gave a positive result, for example, it would cast doubt on the signficance of whatever result may (or may not) have been obtained for PAO*.

It is not apparent that either of the claimed methods is engendered by the demonstration that one of the claimed compounds inhibits L-selectin shedding. While there may be speculation in the literature as to a connection between L-selectin shedding and viral replication, there is no evidence of record showing a correlation between these phenomena. Moreover, it is asserted in the specification (page 8, line 20) that PAO stimulates L-selectin shedding. Accordingly, it is not even clear whether applicants are asserting that compounds which stimulate L-selectin shedding will inhibit viral replication, or whether viral replication is inhibited by compounds which inhibit L-selectin shedding.

The claims that are directed to compounds per se are rejected because each of these claims recites that the compound inhibits PDI, which has not been shown to be the case.

Even if it can be shown that HIV replication is inhibited *in vitro*, it will not follow therefrom that HIV infections in humans can be successfully treated. Each of claims 28-

34 encompasses treatment of HIV infections in humans. The fact is that *in vitro* inhibition of HIV replication is not predictive of an effective therapy in humans. As stated in *Ex parte Forman* (230 USPQ 546, 1986) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. As stated in Mangos (*Texas Medicine*, **86**, 40, 1990):

> "In spite of ... [therapy against HIV and opportunistic infections], the universal outcome of HIV infection / AIDS is the death of the patients" (see, e.g., abstract).

As disclosed in Binquet (*AIDS* **12**, 2313, 1998) a total of 556 patients were treated with HIV protease inhibitors for a period of 230 days, and that despite being treated with with HIV protease inhibitors for more than seven months, 24 of the patients had died. Both of these references teach that death occurs in spite of administration of HIV protease inhibitors. If death is the result of a treatment, one cannot say that success (in the treatment) is predictable.

If sucess is not predictable, it must be "unpredictable". Given that treatment of AIDS is "unpredictable", it follows therefrom that "undue experimentation" would be required to determine which, if any, of the claimed compounds can be used to treat patients afflicted with AIDS. [*Ex parte Balzarini,* 21 USPQ2d 1892)]. Thus, extrapolation from *in vitro* inhibition of viral replication in a petri dish to a therapy in humans is unpredictable.

It is suggested that (a) *in vitro* evidence of HIV replication inhibition be provided, (b) *in vitro* evidence of PDI inhibition be provided, and (c) that claims 28-33 be limited to a method of inhibiting virus replication (or propagation).

*

Claims 2-8, 11, 21-26, 28-33 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 2, there are two substituent variables; however, only one of them is defined. What is the definition of the other (of the two)...?

- In claim 3, there are three substituent variables; however, only one of them is defined. What is the definition of the other two variables?

- Claim 11 mandates that one of R and R' be "uncharged hydrogen" or uncharged alkyl. However, it appears that the term "uncharged" is superfluous in this situation. In traversing, applicants are requested to provide an example of a "charged" hydrogen or a "charged" alkyl.

- Claim 11 mandates that one of R and R' be hydrogen or uncharged alkyl. Claim 2, on which claim 11 depends, permits either of R and R' to be a charged ligand. Thus, for example, claim 2 would permit R to be a charged ligand; at the same time, claim 11 would permit R to be uncharged alkyl. Accordingly, this generates a contradiction.

- Claims 21-26 are indefinite as to the process steps and endpoint. It is suggested that the claims be amended to recite that the cells are exposed to the compound *for a time and under conditions effective to inhibit protein disulfide isomerase (PDI).*

- None of claims 28-33 is enabled, although that is not the point of this rejection. In

the event that evidence is provided that inhibition of viral propagation can be achieved, it is suggested that the claims be amended to recite that the compound be administered *for a time and under conditions effective to inhibit viral propagation.*

- In claims 21-26, the term "PDI" is recited. This term may be used in the claim if accompanied by the full name that this abbreviation represents.

✺

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton. Phone: (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800